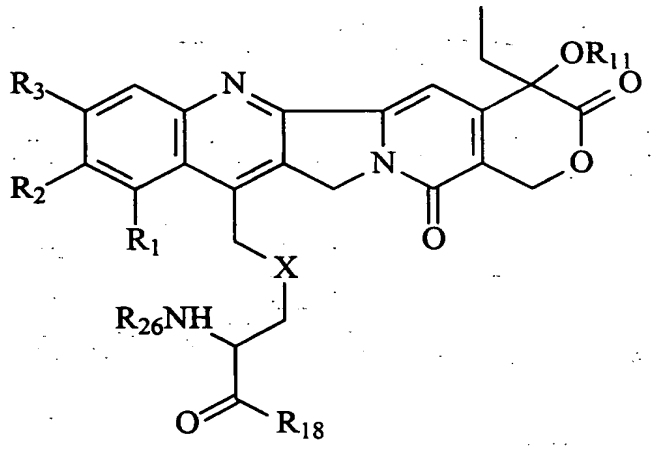
--1. (Twice Amended) A compound comprising:



wherein R_1 and R_2, are each independently

NO_2, NH_2, H, F, Cl, Br, I, COOH, OH, O-C_{1-6} alkyl, SH, S-C_{1-6} alkyl, CN, NH-C_{1-6} alkyl, N(C_{1-6} alkyl)$_2$, CHO, C_{1-8} alkyl, N_3,

-Z-$(CH_2)_a$-N-($(CH_2)_bOH)_2$, wherein Z is selected from the group consisting of O, NH and S, and a and b are each independently an integer of 2 or 3,

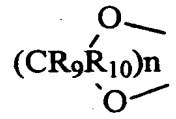
-Z-$(CH_2)_a$-N-(C_{1-6} alkyl)$_2$ wherein Z is selected from the group consisting of O, NH and S, and a is an integer of 2 or 3,

-$CH_2NR_4R_5$, where (a) R_4 and R_5 are, independently, hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-6} alkyl, C_{2-6} alkenyl, hydroxy-C_{1-6} alkyl, C_{1-6} alkoxy-C_{1-6} COR_6 where R_6 is hydrogen, C_{1-6} alkyl, perhalo-C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-6} alkyl, C_{2-6} alkenyl, hydroxy-C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy-C_{1-6} alkyl, or (b) R_4 and R_5 taken together with the nitrogen atom to which they are attached form a saturated 3-7 membered heterocyclic ring which may contain a O, S or NR_7 group, where R_7 is hydrogen, C_{1-6} alkyl, perhalo-C_{1-6} alkyl, aryl, aryl substituted with one or more groups selected from the group consisting of C_{1-6} alkyl, halogen, nitro, amino, C_{1-6} alkylamino, perhalo-C_{1-6} alkyl, hydroxy-

C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy-C_{1-6} alkyl and -COR_8 where R_8 is hydrogen, C_{1-6} alkyl perhalo-C_{1-6} alkyl, C_{1-6} alkoxy, aryl, and aryl substituted with one or more C_{1-6} alkyl, perhalo-C_{1-6} alkyl, hydroxy-C_{1-6} alkyl, or C_{1-6} alkoxy-C_{1-6} alkyl groups;

R_3 is H; or

or R_2 and R_3 combine to form a ring

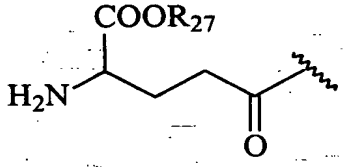


where R_9 and R_{10} are each independently H or F and n is an integer of 1 or 2;

R_{11} is H, or C(O)-$(CH_2)_m$-$NR_{12}R_{13}$, where m is an integer of 1-6 or -C(O)$CHR_{14}NR_{12}R_{13}$, where R_{14} is the side chain of one of the naturally occurring α-amino acids, R_{12} and R_{13} are, independently, hydrogen, C_{1-8} alkyl or -C(O)$CHR_{15}NR_{16}R_{17}$, where R_{15} is the side chain of one of the naturally occurring α-amino acids and R_{16} and R_{17} are each independently hydrogen or C_{1-8} alkyl;

R_{18} is OR_{19} or $R_{19}OC(O)$-$(CH_2)_m$-NR_{20}, or $R_{21}OC(O)CHR_{22}NR_{20}$, where R_{19} is H or C_{1-6} alkyl, m is an integer of 1-6, R_{22} is the side chain of one of the naturally occurring α-amino acids, R_{20} is hydrogen, C_{1-8} alkyl or -C(O)$CHR_{23}NR_{24}R_{25}$, where R_{23} is the side chain of one of the naturally occurring α-amino acids and R_{24} and R_{25} are each independently hydrogen or C_{1-8} alkyl;

R_{26} is H or



where R_{27} is H or C_{1-6} alkyl; and

X is S or O,

or a pharmaceutically acceptable salt thereof.--

SUPPORT FOR THE AMENDMENT

The specification and claims have been amended to remove the proviso clause regarding the present compounds. This does not add new matter, since by the very definition of R18 and R26 in the claims, they cannot both be H, since R18 cannot be H at all. This amendment does not further limit the claims, but merely removes a superfluous line that did not limit the claimed invention.

REQUEST FOR RECONSIDERATION

Applicants' representative would like to thank Examiner Jones for the courteous and helpful discussion of the issues in the present application on September 10, 2002. Applicants would like to thank Examiner Jones for the indication that the claims are allowable over the art of record. The above amendments and following remarks summarize and further expand on the content of that discussion.

The present invention relates to camptothecin compounds having particular substitutions, most notably, at the 7-position on the B ring. In particular, the substituent is a peptide conjugate of an oxymethylene or thiomethylene substituent. Applicants have found that by making these peptide conjugates, the resulting Cpt compounds have significantly increased water solubility, thus increasing their efficacy (i.e. decreasing the dose needed to be effective).

The claims stand rejected under 35 U.S.C. 103 over Miyasaka et al. While it is true that Miyasaka teach various camptothecin derivatives, it is important to note that they do not teach or suggest the peptide conjugates of the present invention. In particular, at the 7-position of interest, Miyasaka have a group X, which can be CH2OR1, with R1 being alkyl or acyl. However, acyl does not cover the peptide group of the present invention, as the

carbonyl group is not attached directly to the oxygen (or sulfur) of the oxymethylene group. Further, Miyasaka nowhere teaches equivalence between the acyl groups taught therein and a peptide group such as that of the present invention. As such, Miyasaka cannot suggest the present invention and the rejection should be withdrawn.

As requested by the Examiner, Applicants have removed the proviso language from the specification and claims, as it did not set forth a meaningful proviso. Applicants further provide herewith an Information Disclosure Statement along with the International Search Report from the corresponding PCT application and a publication of an abstract by the present inventors. The abstract discloses 7-glutathionylmethyl-10,11-methylenedioxy-camptothecin, a compound included in within the present claims. The abstract was published prior to the present application filing date and names two additional co-authors, as well as does not name all of the present co-inventors as co-authors. The subject matter of the abstract that corresponds to the present invention was invented by the present inventors, and the two additional co-authors on the abstract did not inventively contribute to the invention. Applicants note that the co-inventors of the present invention who were not named as co-authors contributed to other aspects of the present invention not disclosed in the abstract.

Applicants submit that this application is now in condition for allowance and early notification of such action is earnestly solicited.

Respectfully submitted,

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